**In the Specification:**

Please amend the specification as shown:

Please delete the paragraph on page 7, lines 13-19 and replace it with the following paragraph:

Targets are immobilized using a c-terminal extension consisting of the peptide sequence (G L N D I F E A Q K I E W H E) **(SEQ ID NO: 1)**, unless the c-terminus is integral to target mechanism of action. In the case where the c-terminus of the target is integral to the target's action the peptide sequence can be added to the n-terminus. This peptide sequence is a substrate for *in vitro* biotinylation using a commercially available enzyme, biotin protein ligase, from Avidity, Denver, CO. The biotin-derivatized target is then immobilized on avidin- or streptavidin-coated microtiter plates.

Please delete the paragraph on page 9, line 22 to page 10, line 2 and replace it with the following paragraph:

Targets are biotinylated and immobilized on streptavidin-coated microtiter plates. The target sequence is modified on the c-terminus to include the sequence (G L N D I F E A Q K I E W H E) **(SEQ ID NO: 1)**, an optimized substrate for biotin protein ligase. The modified target is expressed in a eukaryotic expression system. The c-terminal extension is derivatized with a biotin using biotin protein ligase (Avidity, Denver, CO). The biotin-derivatized target is then immobilized on streptavidin-coated microtiter plates.

Please delete the paragraph on page 15, lines 16-23 and replace it with the following paragraph:

The target (*e,g.*, erythropoietin receptor extracellular hormone binding domain (ERHBD)) is generated with amino-terminal peptide extension (G L N D I F E A Q K I E W H E) **(SEQ ID NO: 1)**. The lysine residue (K) is biotinylated enzymatically (ERHBD*) and the construct is immobilized on

avidin-coated plastic plates. Proper target folding is established by determining epo binding. A combinatorial peptide display library, preadsorbed on avidin coated plates saturated with biotin, is then applied to the immobilized ERHBD*, and those elements of the library associating with the ERHBD* are collected. The collected elements are "phase-one selectants".

Please delete the paragraph on page 20, line 12 to page 22, line 6 and replace it with the following paragraph:

Information, materials, and methods useful in $PPI_{br}$ preparation include:

- The extracellular domain of the human erythropoietin receptor
    - Modifications described in Syed et al (1998) Nature 395:515 for expression in eukaryote expression systems (CHO or Pichia pastoris) is described in Table 1 (the product will be referred to as EPObp) (For the quantities required for the described exercise, the CHO, 293 EBNA, or other cell culture systems will be adequate or are adjusted in a manner known by one of ordinary skill in the art.).
    - An additional alteration to the EPObp is added at the amino terminus to facilitate immobilization of the target EPObp in streptavidin coated microplates. By "alteration" it is meant that: any amino- or carboxyl-terminal change which facilitates immobilization or affixation is usefully (and optionally) included. Alternatively no alteration need be made. Reference is made to optional use of an antibody to the amino-terminal FNIII domain that doesn't interfere with EPO binding.
        - The sequence (G L N D I F E A Q K I E W H E) **(SEQ ID NO: 1)** is added to the amino-terminus of the EPObp. Without being bound by any particular theory it is believed to allow the *in vitro* enzymatic biotinylation of the EPObp in accordance with the recommendations of Avidity (Denver, CO).
    - A panel of EPObp charge-to-alanine mutants is generated. In one embodiment EPObp charge-to-alanine mutants comprise amino acids on the carboxyl-terminal FNIII

domain, with charged side chains that project into the space between the two opposing EPORs in the ternary complex (EPOR-EPO-EPOR). (R=arginine, D=aspartic acid, E=glutamic acid, A=alanine) (see Table 2)

- R130A
- D133A
- E134A
- R141A
- R171A
- E173A
- E176A
- R178A
- E180A
- R187A

- Human erythropoietin (EPO) (unlabled and labeled with $^{125}I$) will be used to establish proper folding of the EPObp constructs by assessing EPO binding isotherms in classical competition assays.

- Bacteriophage peptide display libraries (libraries)
- Conjugated antibodies directed against non-varigated bacteriophage coat proteins for use in detecting bound bacteriophage using a microplate reader.

Please delete Table 1 on pages 25-26 and replace it with the following table:

**Table 1**

EPOR swiss prot accession # p19235

| Key | From | To | Length | Description |
|---|---|---|---|---|
| SIGNAL | 1 | 24 | 24 | |
| CHAIN | 25 | 508 | 484 | ERYTHROPOIETIN RECEPTOR. |
| DOMAIN | 25 | 250 | 226 | EXTRACELLULAR (*POTENTIAL*). |
| TRANSMEM | 251 | 273 | 23 | *POTENTIAL*. |
| DOMAIN | 274 | 508 | 235 | CYTOPLASMIC (*POTENTIAL*). |
| DOMAIN | 148 | 213 | 66 | FIBRONECTIN TYPE-III. |
| DISULFID | 52 | 62 | | |
| DISULFID | 91 | 107 | | |
| CARBOHYD | 76 | 76 | | N-LINKED (GLCNAC...) (*POTENTIAL*) |

```
    10       20       30       40       50       60
    |        |        |        |        |        |
MDHLGASLWP QVGSLCLLLA GAAWAPPPNL PDPKFESKAA LLAARGPEEL LCFTERLEDL

    70       80       90       100      110      120
    |        |        |        |        |        |
VCFWEEAASA GVGPGNYSFS YQLEDEPWKL CRLHQAPTAR GAVRFWCSLP TADTSSFVPL

    130      140      150      160      170      180
    |        |        |        |        |        |
ELRVTAASGA PRYHRVIHIN EVVLLDAPVG LVARLADESG HVVLRWLPPP ETPMTSHIRY

    190      200      210      220      230      240
    |        |        |        |        |        |
EVDVSAGNGA GSVQRVEILE GRTECVLSNL RGRTRYTFAV RARMAEPSFG GFWSAWSEPV

    250      260      270      280      290      300
    |        |        |        |        |        |
SLLTPSDLDP LILTLSLILV VILVLLTVLA LLSHRRALKQ KIWPGIPSPE SEFEGLFTTH

    310      320      330      340      350      360
    |        |        |        |        |        |
KGNFQLWLYQ NDGCLWWSPC TPFTEDPPAS LEVLSERCWG TMQAVEPGTD DEGPLLEPVG
```

370 380 390 400 410 420
SEHAQDTYLV LDKWLLPRNP PSEDLPGPGG SVDIVAMDEG SEASSCSSAL ASKPSPEGAS

430 440 450 460 470 480
AASFEYTILD PSSQLLRPWT LCPELPPTPP HLKYLYLVVS DSGISTDYSS GDSQGAQGGL

490 500
SDGPYSNPYE NSLIPAAEPL PPSYVACS **(SEQ ID NO: 2)**
EPOR construct as described in Syed et al 1998 Nature 395:515
A25 redefined as aa#1
specific mutations shown in red: N52Q, N164Q, and A211E
The ala, shown in orange was replaced by arg-glu-phe (REF)

10 20 30 40 50 60
~~MDHLGASLWP QVGSLCLLLA GAAW~~APPPNL PDPKFESKAA LLAARGPEEL LCFTERLEDL

70 80 90 100 110 120
VCFWEEAASA GVGPGQYSFS YQLEDEPWKL CRLHQAPTAR GAVRFWCSLP TADTSSFVPL

130 140 150 160 170 180
ELRVTAASGA PRYHRVIHIN EVVLLDAPVG LVARLADESG HVVLRWLPPP ETPMTSHIRY

190 200 210 220 230 240
EVDVSAGQGA GSVQRVEILE GRTECVLSNL RGRTRYTFAV RARMAEPSFG GFWSEWSEPV

250 260 270 280 290 300
SLLTPSDLDP ~~LILTLSLILV VILVLLTVLA LLSHRRALKQ KIWPGIPSPE SEFEGLFTTH~~

310 320 330 340 350 360
~~KGNFQLWLYQ NDGGLWWSPC TPFTEDPPAS LEVLSERCWG TMQAVEPGTD DEGPLLEPVG~~

370 380 390 400 410 420
~~SEHAQDTYLV LDKWLLPRNP PSEDLPGPGG SVDIVAMDEG SEASSCSSAL ASKPSPEGAS~~

430 440 450 460 470 480

~~AASFEYTILD PSSQLLRPWT LCPELPPTPP HLKYLYLVVS DSGISTDYSS GDSQGAQGGL~~

~~SDGPYSNPYE NSLIPAAEPL PPSYVAGS~~ **(SEQ ID NO: 3)**

Please delete Table 2 on pages 27-28 and replace it with the following table:

**Table 2**

Charge to alanine EPObp mutants//those amino acids depicted in red will be individually changed to alanine

~~MDHLGASLWP QVGSLCLLLA GAAW~~APPPNL PDPKFESKAA LLAARGPEEL LCFTERLEDL

VCFWEEAASA GVGPGQYSFS YQLEDEPWKL CRLHQAPTAR GAVRFWCSLP TADTSSFVPL

ELRVTAASGA PRYHRVIHIN EVVLLDAPVG LVARLADESG HVVLRWLPPP ETPMTSHIRY

EVDVSAGQGA GSVQRVEILE GRTECVLSNL RGRTRYTFAV RARMAEPSFG GFWSEWSEPV

SLLTPSDLDP ~~LHLTLSLHLV VILVLLTVLA LLSHRRALKQ KIWPGIPSPE SEFEGLFTTH~~

~~KGNFQLWLYQ NDGCLWWSPC TPFTEDPPAS LEVLSERCWG TMQAVEPGTD DEGPLLEPVG~~

370 380 390 400 410 420

~~SEHAQDTYLV LDKWLLPRNP PSEDLPGPGG SVDIVAMDEG SEASSGSSAL ASKPSPEGAS~~

430 440 450 460 470 480

~~AASFEYTILD PSSQLLRPWT LCPELPPTPP HLKYLYLVVS DSGISTDYSS GDSQGAQGGL~~

490 500

~~SDGPYSNPYE NSLIPAAEPL PPSYVAGS~~ **(SEQ ID NO: 4)**